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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,309	01/03/2001	Christine Andreoni	PF82PCTSEQ/d	7033

25666 7590 10/11/2005

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,309	ANDREONI ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24 and 26-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24 and 26-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Response to Amendment

The response filed 4-19-05 has been entered into the record. Claims 22-24 and 26-39 are pending and under examination. A complete review of the electronic prosecution record has been performed and it appears that the copy of the replacement drawings filed 4-8-03 by Applicant is missing from the electronic file. The current examiner respectfully requests a second copy of the replacement drawings for scanning purposes in order to complete the record.

Please note that the examiner in charge of this Application has changed. Please address all future correspondence to Exr. Patricia A. Duffy, Art Unit 1645.

All rejections of record are withdrawn in view of the new grounds of rejection set forth below.

Claim Objections

Claims 22-24, 26-39 are objected to because of the following informalities: The claims lack a conventional transitional phrase and lack active method steps. Appropriate correction is required. This issue may be resolved by amending the claims to recite "A method of improving systemic immunity of a mammal with respect to an antigen or hapten comprising administering to the mammal an immunologically effective amount of a pharmaceutical composition comprising ..."

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 22-24, 26-28 and 39 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed invention is drawn to a natural process of nature. The process of nature is the natural infection of mammals by Klebsiella pneumoniae because Klebsiella pneumoniae inherently possesses the recited OmpA/P40/SEQ ID NO:2 and other antigens or haptens and natural infection occurs via the respiratory (nasal) route. Therefore, the method does not reflect the "hand of man" in the process or product that is administered. This issue may be resolved by amending the pharmaceutical composition administered to reflect the hand of man in the antigens purity. The process limitations of claims 23 and 24 do not distinguish from the natural OmpA/P40/SEQ ID NO:2 produced by Klebsiella pneumoniae.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24, 26-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

The claims recite a method of improving systemic immunity. The specification fails to provide conception for "systemic immunity". The concept of "Systemic Immunity" is not set forth by way of written description in the specification as filed. Systemic includes both antigen specific and non-specific responses (activation of antigen processing cells; activation of NK cells; polymorphs). The antigen specific response involve both humoral (antibody; complement) and cellular responses (T-helper, T-cytotoxic or T-suppressor cells). The teachings of the specification are limited to a showing of intranasal administration of a recombinant protein comprising SEQ ID NO:2-G' (RSV) and the generation of different isotypes of antibodies (IgG2 versus IgG1) with respect to a Th1 and Th2 response, but does not address or contemplate a discrimination between local and systemic immunity (see page 14, section 5.4). This issue is best resolved by Applicants pointing to the specification by page and line number where conception by way of written description can be found for the this new claim limitation.

Claims 22-24 and 26-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 22 and every claim dependent thereon (23, 24 and 26-39), the claims are *prima facie* indefinite in the use of improving systemic immunity because there is no baseline for comparison and as such the metes and bounds of "improved" cannot be ascertained by the skilled artisan and the skilled artisan would be unable to ascertain if they were infringing upon the claim. Further, the claim is prima facie indefinite because "the Klebsiella pneumoniae protein" lacks clear antecedent basis in the claims. The latter issue may be resolved by amending the claims to recite "a pharmaceutical composition

comprising an isolated Klebsiella penumoniae OmpA membrane protein wherein the OmpA membrane protein comprises the amino acid sequence as set forth in SEQ ID NO:2....".

As to claim 26, the claim recites "proteins or peptides" and the difference in the metes and bounds of these terms are not defined in the specification or claims. As such, the skilled artisan would not be readily apprises of the metes and bounds of these terms.

As to claims 35-38, the claims are confusing because they are unclear process steps written in past tense. If applicants intend to limit the product by specific process limitations the process limitations should be clearly delineated.. or applicants should specifically structurally limit the agent that couples (i.e. wherein the covalently coupled OmpA antigen or hapten are coupled by one or more bonding elements). The current combination of processes of making that are incomplete lead to indefinite structural limitations of the pharmaceutical composition administered.

As to claim 39, the claim is prima facie indefinite because it is not the method that does not contain an adjuvant, but the pharmaceutical composition. If applicants intend to limit the method then they should indicate a process limitation rather than a structural limitation of the pharmaceutical composition.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-24, 26-28 and 39 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cooper et al (The Journal of Infectious Diseases, 147(2):312-317).

Cooper et al teach intranasal immunization of a mammal (mouse) with gluteraldehyde-killed *Klebsiella pneumoniae*. The whole cell vaccine inherently comprises the claimed OmpA having the amino acid sequence set forth in SEQ IDNO:2 in combination with an antigen or hapten. The whole cell vaccine inherently comprises proteins, peptides, polysaccharides, oligosaccharides and nucleic acids. Cooper et al teach that the intranasal administration increased produced IgA antibodies in the serum as compared to a non-

vaccinated control. As such, the intranasal administration improved systemic immunity in the mouse as compared to a non-immune control.

Claims 22-24 and 26-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rauly et al (Research in Immunology, 149(1):pp 99, January 1998) in view of Gizurarson et al (Vaccine Research 6(1):41, 1997; abstract only), Waldo et al (Clinical Immunology and Pathology, 72(1):30, 1994; Abstract only) and Aggerbeck et al (Vaccine 15(3):307-316, 1997).

Rauly et al teach a method of using an outer membrane protein (OmpA) of Klebsiella pneumoniae for enhancing or improving immunity of a mammal with respect to an antigen or hapten (page 99). Rauly et al teach an OmpA protein of *K. pneumoniae* produced by a recombinant process (rP40). Rauly et al teach the use of G1 antigen of RSV coupled to the rP40, the same conjugate as the claimed invention is as effective as a tetanus toxin G1 conjugate and the rP40-G1 conjugate was effective to produce antibodies in the absence of adjuvant. The coupled protein of the prior art having the same name, structural properties, produced from the same microorganism, the same institute by the same group of scientists is innately the same conjugate as claimed. The claimed process steps (claims do not distinguish the product of Rauly from the claimed product or its functionality (i.e. ability to induce a systemic immune response). Rauly et al differ by not intranasally administering the rP40-G1 conjugate.

Gizurarson et al teach that "Animal studies have shown that intranasal administration of vaccines can induce an immune response equivalent to that with subcutaneous injection...."(see abstract).

Waldo et al teach that "Intranasal administration immunization results in both a mucosal and systemic immune response in humans."

Aggerbeck et al teaches that amount 215 persons immunized intranasally 61% preferred the intranasal route of administration as compared to a parenteral injection (see abstract page 307)

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to administer the rP40-G1 conjugate of Rauly et al by the intranasal route because both Gizurarson et al and Waldo et al teach that intranasal immunization in animals, including humans, results in an immune response equivalent to that by subcutaneous immunization and results in both a mucosal and systemic immune response and Aggerbeck et al teach that intranasal immunization was preferred in a population of individuals as compared to injection and finally, intranasal provides the immediate and obvious benefits in a reduction of pain associated with injection needles, increased safety for health care workers due to lack of potential needle sticks, ease, safety and low cost.

Relevant Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Waldo et al (Journal of Clinical and Laboratory Immunology, 34(3):p 125 (abstract only) March 1991 is cited to teach that nasal immunization can result in a systemic IgA response.

Hu et al (Journal: Clinical and experimental immunology, 113(2):235-243, 1998) is cited to teach that RSV envelope proteins in combination with ISCOMs when administered intranasally induced a higher and longer lasting IgM and IgG1 response as compared to subcutaneous administration (see abstract).

DiTommaso et al (Infection and Immunity, 64(3):974-979, March 1996) is cited to teach that intranasal vaccination produces a systemic antibody response (see abstract).

Russell et al (Infection and Immunity, 64(4):1272-1283, April 1996) is cited to teach that intranasal vaccination produces a systemic antibody response when an antigen is either combined or fused with the cholera toxin B subunit.

Wu et al (Vaccine, 16(1-2):286-92, Jan-Feb 1998) is cited to teach a systemic and mucosal response is elicited to a heterologous protein antigens administered by the intranasal route.

Status of the Claims

All claims stand rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy, Ph.D.

Primary Examiner

Art Unit 1645